



Central Pattern Generators

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Central pattern generators (CPGs) are neural networks that can produce rhythmic patterned outputs without rhythmic sensory or central input. CPGs underlie the production of most rhythmic motor patterns and have been extensively studied as models of neural network function.

Introduction

A central goal of neuroscience is to understand how nervous systems produce movement. The simplest movements are reflexes (knee jerk, pupil dilation), which are involuntary, stereotyped and graded responses to sensory input, and have no threshold except that the stimulus must be great enough to activate the relevant sensory input pathway. Fixed action patterns (sneezing, orgasm) are involuntary and stereotyped, but typically have a stimulus threshold that must be reached before they are triggered, and are less graded and more complex than reflexes. Rhythmic motor patterns (walking, scratching, breathing) are stereotyped and complex, but are subject to continuous voluntary control. Directed movements (reaching) are voluntary and complex, but are generally neither stereotyped nor repetitive.

Rhythmic motor patterns comprise a large part of behaviour. They are also complex (unlike reflexes) yet stereotyped (unlike directed movements) and, by definition, repetitive (unlike fixed action patterns). As a consequence of this combination of behavioural importance and experimental advantage, rhythmic motor pattern generation has been studied extensively. This work has shown that the basic rhythmicity and patterning of rhythmic motor patterns are produced by neural networks termed central pattern generators.

What is a Central Pattern Generator?

Central pattern generators (CPGs) are neural networks that can endogenously (i.e. without rhythmic sensory or central input) produce rhythmic patterned outputs; these networks underlie the production of most rhythmic motor patterns ([Marder and Calabrese, 1996](#); [Stein et al., 1997](#)). The first modern evidence that rhythmic motor patterns are centrally generated was the demonstration that the locust nervous system, when isolated from the animal, could produce rhythmic output resembling that observed during flight (Wilson, 1961 cited in [Marder and Calabrese, 1996](#)). Subsequent work showed that, in a wide variety of animals, nervous systems isolated from sensory feedback could produce rhythmic outputs resembling those observed during rhythmic motor pattern production. This work has further shown that rhythmic pattern generation does not depend on the nervous system acting as a whole, but that CPGs are instead relatively small and autonomous neural networks.

Concept of Fictive Motor Patterns

A fictive motor pattern is a pattern of motor neuron firing that would, if the motor neurons were still attached to their muscles, result in the motor pattern in question being produced. This concept arose because the best evidence for CPGs comes from work on isolated nervous systems. However, these preparations raise a question: is the neural activity observed *in vitro* the same as that which generates the motor pattern observed *in vivo*? An unambiguous demonstration has been achieved in only a few invertebrate preparations in which the CPG and the muscles it innervates can be simultaneously maintained *in vitro*, and it can be shown that a given neural output pattern induces a specific motor output. Only slightly less ambiguous are preparations (again primarily invertebrate) in which the motor nerves contain sufficiently few axons that the activity of each motor neuron can be identified *in vivo* from chronic extracellular nerve recordings; *in vivo* and *in vitro* motor neuron activity can thus be compared directly.

In preparations with nerves that have large numbers of axons, it is more difficult to show that the same motor neurons are active *in vivo* and *in vitro*. In these cases, demonstrating that correct nerve activity continues *in vitro* (e.g. flexor and extensor motor neuron activities maintain the correct phase relationship), without showing that identical motor neurons are firing, is often considered sufficient evidence of a correct fictive motor pattern.

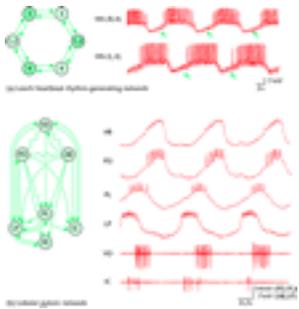
Basic Mechanisms for the Generation of Patterned Rhythmicity

All rhythms require: (1) two or more processes that interact such that each process sequentially increases and decreases, and (2) that, as a result of this interaction, the system repeatedly returns to its starting condition. Consider a pendulum at the moment of release. At this time, the pendulum bob's gravitational potential energy is at its maximum and the bob's momentum is zero. If the bob were not attached to the pendulum arm, when the bob was released it would simply fall: its potential energy would decrease monotonically, and its momentum would increase monotonically, until it hit the ground. However, the pendulum arm constrains the bob to move in a semicircular path. This constraint links the bob's potential energy and momentum such that, as the bob descends, its momentum increases and its potential energy decreases until, at the bottom of the swing (when the pendulum arm is vertical), these two quantities reach their respective maximum and minimum. At this time the bob's momentum forces the bob to ascend the other arm of its trajectory, and as its momentum decreases its potential energy increases until again (at the other highest point of its swing) its momentum is zero and its potential energy is maximum. The bob then descends, momentum and potential energy coordinately increase and decrease (on the downswing), and decrease and increase (on the upswing), until the bob reaches its original starting point, at which point the cycle repeats.

The task at hand, therefore, consists of identifying the processes and interactions that underlie neurally generated rhythms. Neural rhythmicity arises either through interactions among neurons (network-based rhythmicity) or through interactions among currents in individual neurons (endogenous oscillator neurons). A clear example of network-based rhythmicity is provided by the leech heartbeat CPG. This network is unusual in that it can be divided into two subsets, one of which (the rhythm generator)

produces the pattern's basic rhythm and the other of which (the pattern generator), in response to driving input from the rhythm generator, generates the actual motor pattern.

[Figure 1a](#), left, shows the rhythm generator's synaptic connectivity. The network consists of four bilaterally symmetrical neuron pairs. The right and left 3 and 4 neurons inhibit each other, and on each side neurons 1 and 2 are reciprocally inhibitory with neurons 3 and 4; the network thus forms a ring of reciprocally inhibitory neuron pairs. [Figure 1a](#), right, shows simultaneous intracellular recordings from right and left neurons 4; it is apparent that they rhythmically fire precisely out of phase (antiphase). Recordings from other network neurons show that the 3 and 4 neurons on one side fire synchronous action potential bursts with the 1 and 2 neurons on the other side. The network thus produces a two-phase rhythm in which the open and closed neurons (left) burst in antiphase.



[Figure 1](#)

Mechanisms for central pattern generator rhythmicity. (a)

Network-based rhythmicity (the leech heartbeat rhythm generator).

The network (left) consists of a ring of six neurons interconnected by reciprocally inhibitory synapses (stick-and-ball connectors).

Particularly important are the neuron 3 and 4 pairs, each of which forms a half-centre oscillator (see text). The neurons of each pair burst in antiphase (right). The 1 and 2 neurons form a coordinating link between the neuron 3 and neuron 4 half-centres; the network thus produces a two-phase pattern in which the open and closed neurons burst in antiphase (left). Arrows indicate the slow depolarization that allows the off-neuron to escape from inhibition

(see text). Modified from Marder and Calabrese (1996). (b) A

network (the lobster pyloric network) driven by an endogenous oscillator neuron. Left: The network's neuronal complement and synaptic interconnectivity (inhibitory synapses, stick-and-ball connectors; electrical coupling, resistors; rectifying electrical coupling, diode). The AB neuron is an endogenous oscillator neuron, and under most circumstances is the network's rhythmic driver. AB

neuron input induces postinhibitory rebound and plateaux in its follower neurons and, as a consequence of these effects and the interactions among the follower neurons, the network produces a multiphasic rhythmic neural output (right). Left panel modified from Harris-Warrick *et al.* (1992); right panel from author's laboratory.

Neurons not identified in text: VD, Ventricular Dilator; PL, Pyloric Late; PE, Pyloric Early.

Key to understanding rhythm generation in this (and many other network-based CPGs) is the concept of a half-centre oscillator. A half-centre oscillator consists of two neurons that individually have no rhythmogenic ability, but which produce rhythmic outputs when reciprocally coupled. Several types of interacting processes can support this rhythm generation (see below), but first I shall describe the specific mechanism that functions in the leech heartbeat network.

Considering only the reciprocally inhibitory neuron 4 pair, imagine that firing by one of the neurons not only inhibits the other neuron, but also induces the other neuron slowly to escape from inhibition. In this case, rhythmogenesis could arise as follows. Initially, one neuron, say the right, is firing. This activity inhibits the left neuron, but also induces a slow depolarization in it, and eventually the left neuron reaches spike threshold and begins to fire. Firing in the left neuron inhibits and stops the right neuron from firing, but again also induces a slow depolarization in it. The right neuron therefore eventually reaches spike threshold and begins to fire. This activity inhibits and stops the left neuron from firing, and the cycle repeats.

In the leech heartbeat rhythm generator, this process is now understood on the current level. Key to it are a hyperpolarization-activated inward current (I_h) and a low-threshold persistent Na^+ current (I_p) in neurons 4 ([Olson et al., 1995](#)). In the neuron being inhibited (the off-neuron), this hyperpolarization gradually turns on I_h , and consequently the off-neuron slowly depolarizes (note the slow depolarization of the neurons during their inhibitions; arrows). When the threshold of I_p is crossed, the off-neuron escapes from inhibition, begins to fire, and inhibits the neuron that had been firing. I_h now begins to turn on in this new off-neuron; eventually the threshold of I_p is crossed, the new off-neuron escapes from inhibition, and the process repeats.

Rhythmogenesis in the leech heartbeat rhythm generator thus occurs as follows. Both neurons of the neuron 3 and neuron 4 pairs possess I_h and I_p , and each neuron pair forms a functional half-centre in which the two neurons burst in antiphase. Neurons 1 and 2 reciprocally inhibit the ipsilateral 3 and 4 neurons, and hence the only stable mode of bursting for the neurons of one side is for the 3 and 4 neurons to burst together and in antiphase with neurons 1 and 2; this results in the entire network having the activity shown in [Figure 1a](#), right. The neuron 3 and 4 half-centres form the rhythmic heart of the network, and the 1 and 2 neurons coordinate the activity of these two half-centres ([Marder and Calabrese, 1996](#)).

Reciprocal inhibition is very common in CPG networks, and half-centre oscillators have been modelled extensively. This work has revealed that half-centres can function in a variety of ways. First, the two neurons of the half-centre need not fire in antiphase. Depending on the dynamics of synaptic release, any relative phasing, even synchronous firing, of the neurons can be achieved ([Van Vreeswijk et al., 1994](#)). Second, in addition to the ‘escape’ mechanism described above, half-centres can also function in a ‘release’ mode in which, as a consequence of its intrinsic properties, the on-neuron stops firing of its own accord. In this mode the off-neuron turns on not by escape from inhibition, but instead simply by being released from it. These modes can be further subdivided depending on whether the transitions occur because neuron firing state changes (intrinsic escape or release) or because (before neuron firing changes) the neurons cross voltage thresholds governing synaptic transmitter release (synaptic escape or release). In each mode the half-centre functions differently, and half-centres can be shifted among modes by changes in synaptic release threshold ([Skinner et al., 1994](#)). Variations in synaptic properties can thus dramatically alter half-centre activity, and this flexibility may partially underlie the ability of CPGs to produce multiple output patterns (see Modulation of central pattern generators, below).

A network that, under most circumstances, is driven by an endogenous oscillator neuron is the pyloric network (the CPG that generates movements of the pylorus, the most posterior region of the stomach) of decapod crustacea such as lobsters and crabs ([Harris-Warrick et al., 1992](#)). [Figure 1b](#) shows the

network's synaptic connectivity (left) and neural output (right). The Anterior Burster (AB) neuron is an endogenous oscillator: even when isolated from the network, it rhythmically depolarizes, fires a burst of action potentials, repolarizes, and then depolarizes again to repeat the cycle. In the case of endogenous oscillators, the interacting processes that produce the rhythm are membrane currents. Many sets of currents can do so, but a simple example of how this could occur is as follows. Imagine a neuron that possesses, in addition to standard action potential generating currents, a low-threshold, noninactivating, voltage-activated Ca^{2+} current (I_{Ca}), a Ca^{2+} -activated K^+ current (I_{KCa}) and a leak current (I_{L}) whose reversal potential is more depolarized than the activation voltage of I_{Ca} . If we start at a membrane potential more hyperpolarized than the activation voltage of I_{Ca} , the neuron depolarizes towards the reversal potential of I_{L} . The Ca^{2+} channels open when the membrane potential reaches the activation voltage of I_{Ca} , and the neuron strongly depolarizes and fires action potentials. I_{KCa} grows as Ca^{2+} enters the neuron, and the neuron hyperpolarizes. Eventually the membrane potential becomes more hyperpolarized than the activation voltage of I_{Ca} , I_{Ca} ceases, the membrane potential drives toward the K^+ reversal potential, and the neuron stops firing. As Ca^{2+} concentration drops due to Ca^{2+} sequestration and extrusion, I_{KCa} drops, the neuron again begins to depolarize toward the reversal potential of I_{L} , and the cycle repeats.

With respect to pattern generation in the pyloric network, the relative phasing of the network's neurons is determined by the network's synaptic connectivity, the dynamics of the various synapses, and the intrinsic membrane properties of the neurons. The pyloric dilator (PD) neurons are electrically coupled to the AB neuron, and hence fire in phase with it. All the other neurons are inhibited by the PD and/or AB neurons, and thus fire out of phase with them. These neurons all possess hyperpolarization-activated depolarizing currents, and show a rebound depolarization (postinhibitory rebound; PIR) after this inhibition. This depolarization activates additional inward currents that induce a long-lasting depolarization (plateau) and burst of action potentials. The Lateral Pyloric (LP) and Inferior Cardiac (IC) neurons fire first after the AB and PD neurons because they have the most rapid PIR; the other neurons fire later because their PIR is slower and because they are delayed by inhibition from the LP and IC neurons.

It is important to note several generally applicable aspects of this network. First, the AB neuron receives direct or indirect input from all the network's neurons, and changes in any neuron's activity can alter network cycle period. It is thus impossible to divide the network into rhythm-generating and pattern-creating subsets. This confounding of rhythm and pattern generation can be clearly shown by removing the AB neuron from the network, in which case (as a result of the network's multiple half-centres) a pattern similar to that produced by the intact network continues. Thus, although the network has an endogenous oscillator, the extent to which network rhythmicity is endogenous oscillator or network based presumably varies as a function of the intrinsic properties of the network's neurons and synapses (see Modulation of central pattern generators, below). Second, note the network's bewildering complexity; it is impossible to predict the network's output merely by looking at its synaptic connectivity. Similar complexity is present in almost all CPGs known on the cellular level. Third, note the presence here and in the leech of neurons with 'complicated' intrinsic properties (endogenous oscillation, PIR, plateaux). Neurons with such properties are present in all CPGs known on the cellular level.

Multilimb and Multisegment Coordination

Limb and segment movements are coordinated during multilimb–segment behaviours such as terrestrial locomotion and undulatory swimming. Experiments in which central nervous systems are progressively isolated suggest that, although sensory feedback and the mechanical properties of the musculoskeletal system contribute to this coordination, it also arises in part from central mechanisms. Experiments in limbed vertebrates have shown that individual limbs can produce stepping movements, and experiments in lamprey and leech have shown that a few or even individual segments can produce a basic swimming motor pattern. These data have been interpreted as evidence that each limb, and each or at most a few segments, have their own CPG (a unit oscillator), and that central coordination among limbs and segments arises from coordinating connections among these oscillators.

Considerable theoretical work has been performed for the case of weak interoscillator coupling, and some of these predictions have been observed experimentally, particularly in the lamprey ([Grillner *et al.*, 1991](#); [Cohen *et al.*, 1992](#)). However, it is important to note that in some systems (e.g. the leech) the strength of the interoscillator coupling is as great as that inside the unit oscillators. The effects of strong coupling on unit oscillator activity, and even whether the unit oscillators would maintain identifiably separate identities when so coupled, is less understood.

Role of Sensory Feedback in Central Pattern Generation

One role of sensory feedback is to alter motor patterns to deal with environmental perturbations (corrective input). This process is difficult because, to preserve function, certain motor pattern coordination relationships may need to be maintained, changes in one part of the pattern may therefore require compensatory changes in other parts of the pattern, and thus many movements may change even though the sensory input occurs during only one phase of the pattern. For instance, consider walking with a pebble in the heel of the right shoe (right leg limping). The sensory input is active only during right leg stance. However, it induces global changes in walking that include decreased right knee extension and maintained right ankle flexion during times (right leg swing) when the sensory input is inactive. Little is known about how this holistic CPG targeting is achieved. One way it could occur is by the input having widespread and long-lasting effects. An alternative possibility is that the input affects only a few CPG neurons and has only short-acting effects, but induces global, long-lasting motor pattern changes because the activity changes of the directly targeted neurons induce changes in their followers, which induce changes in their followers, etc. CPGs would thus have evolved so that, in response to sensory input, the network could assume multiple configurations that produced different outputs (see Modulation of central pattern generators, below).

A related difficulty is that the effect of a sensory input will often vary depending on the phase of the motor pattern in which it is given. For instance, if in walking the foot encounters resistance (a horizontally projecting stick) during swing, the behaviourally correct response is to lift the leg higher and step over the stick. It would be extremely disadvantageous if, during stance, the identical sensory input (a tap to the top of the foot) caused the leg to lift, because at this time the contralateral leg is in the swing phase: the animal would collapse. If anything, during stance, it would be most advantageous if the input

caused the leg to descend to enhance stability by increasing the force between the foot and the substrate. This change in motor response as a function of motor pattern phase is called reflex reversal, and has been observed in invertebrates ([DiCaprio and Clarac, 1981](#)) and vertebrates ([Forssberg *et al.*, 1977](#)). How this process occurs is poorly understood, but again two possibilities exist. One is that sensory input is appropriately routed to different CPG neurons as a function of motor pattern phase. The other is that the input reaches the same neurons at all phases, but that, as a consequence of the way in which the network transforms the input, network response varies appropriately as a function of motor pattern phase.

A conceptually different role of sensory feedback (although in practice these afferents would also be active in corrective responses) is to contribute to CPG activity in an ongoing fashion during normal, unperturbed, motor pattern production ([Wolf and Pearson, 1988](#)). The left panel of [Figure 2a](#) shows the output of a locust flight elevator motor neuron with sensory feedback intact; the right panel shows the output of the same neuron after sensory feedback has been removed (deafferented). It is apparent that deafferentation increases pattern cycle period and neuron burst duration. [Figure 2b](#) shows an experiment in which a flight sensory feedback afferent, the forewing stretch receptors (FSRs), was stimulated electrically (upward lines on bottom trace) at the physiologically appropriate phase in the neural pattern. FSR stimulation rapidly decreased cycle period and neuron burst duration, and resulted in a pattern similar to that observed in intact animals (compare with the left panel in [Figure 2a](#)).

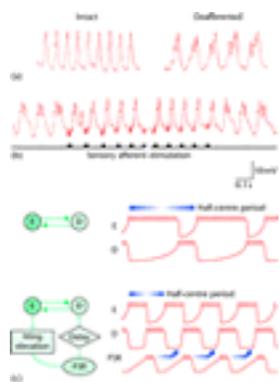


Figure 2

Sensory feedback can contribute to central pattern generator activity during normal motor pattern production. (a) Recordings of elevator motor neuron activity during locust flight with (left) and without (right) intact sensory feedback. Cycle period and burst duration increase in the deafferented preparation. (b) Sensory afferent stimulation (black rectangles on bottom trace) in deafferented locusts decreases cycle period and elevator motor neuron burst duration to near normal levels; compare with left panel in (a). (c) A simplified version of the mechanisms underlying the sensory feedback effects. The elevator and depressor interneurons form a half-centre oscillator with a long cycle period and long elevator bursts (top). Wing elevation activates a sensory receptor, the forewing stretch receptor (FSR), which excites, with a delay, the depressors (bottom). This input induces the depressors to fire earlier than they otherwise would, which decreases elevator burst duration and cycle period. Inhibitory synapses are shown with stick-and-ball connectors, excitatory synapses with stick-and-bar connectors. (a) and (b) modified from [Wolf and Pearson \(1988\)](#); (c) modified from [Pearson and Ramirez \(1990\)](#).

[Figure 2c](#) shows a simplified version of the mechanisms believed to underlie these effects ([Pearson and Ramirez, 1990](#)). To a first approximation, the flight CPG functions as a half-centre oscillator. In the absence of sensory input ([Figure 2c](#), top) the depressor interneurons depolarize only slowly, and elevator interneuron burst duration and cycle period are long. The FSRs are activated at peak wing elevation, and

thus fire at the beginning of depressor firing. The FSRs excite the depressors, but only after a considerable delay. As a result, although the FSRs and the depressors fire nearly simultaneously, the FSRs do not excite the depressors until well into the depressor postburst hyperpolarization. This excitation induces the depressors to fire earlier, which reduces elevator burst duration and hence decreases cycle period.

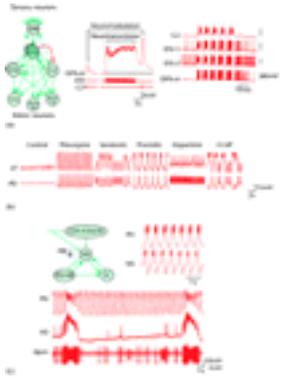
Similar results in which contributory sensory feedback alters motor pattern cycle period and/or phasing have been obtained in several systems. Note that these results do not contradict the theory of central pattern generation: basic rhythmicity and patterning are still centrally generated. Nonetheless, it is increasingly clear that behaviourally appropriate (i.e. with correct cycle period and phasing) rhythmic motor patterns often cannot be produced without intact contributory sensory feedback.

Modulation of Central Pattern Generators

Neural transmission can be classical or modulatory. In classical transmission, neurotransmitter binds to a receptor–ion channel complex and leads directly to a change in the open state of the associated channel. The postsynaptic response occurs quickly and typically last for tens of milliseconds (the duration of binding of the transmitter to the receptor). Modulatory transmission results from neurotransmitter binding to a receptor that only indirectly alters ion channel activity. There are one or more intermediate steps, commonly beginning with activation of a guanosine triphosphate (GTP)-binding protein, and often including a second messenger-mediated cascade which changes the phosphorylation state of the channel and so alters channel function (e.g. voltage sensitivity). The postsynaptic response can last from hundreds of milliseconds to hours. A notable recent development in neurobiology is an increasing awareness of the importance of modulation in nervous system function; over the past decade, scores of modulators have been identified. Much of this work has been performed in CPGs, and our best understanding of the mechanistic bases of neural network modulation comes from these systems. Three roles of modulation in CPG function have been identified.

The first role is the use of modulators in the CPG as a part of its normal activity ([Katz and Frost, 1996](#)). [Figure 3a](#), left, shows the synaptic connectivity of the *Tritonia* swimming CPG. In response to weak sensory input, the network helps produce reflexive withdrawal; in response to stronger input, it generates swimming ([Figure 3a](#), right). Part of this flexibility is due to release by the dorsal swim interneurons (DSI) neurons of a modulatory transmitter, serotonin, which induces neuron cerebral cell 2 (C2) to release more transmitter and hence strengthens its synapses in the network ([Figure 3a](#), middle). Application of serotonergic antagonists prevents the network from producing the swimming pattern, and hence this intranetwork modulation appears essential for network oscillation.

Figure 3



Central pattern generator (CPG) modulation. (a) Intrinsic modulation. The *Tritonia* swimming CPG contains neurons, the DSI neurons, which, in addition to their classical synapses (green connections), release a modulator (serotonin; red arrow) (left). Sustained DSI neuron firing results in increased neuron C2 synaptic strength (middle). In response to strong sensory input (arrow) the network produces a fictive swimming pattern (right); if the serotonergic modulation is blocked pharmacologically, fictive swimming is also blocked (not shown). Inhibitory synapses, stick-and-ball connectors; excitatory synapses, stick-and-triangle connectors; mixed inhibitory–excitatory synapses are shown with a combination. Modified from Katz and Frost (1996). Neurons not identified in text: DRI, dorsal ramp interneuron; VSI, ventral swim interneuron; VFN, ventral flexion neuron; DFN-A, DFN-B, dorsal flexion neurons A and B (b) Single neural networks can produce multiple outputs. The panels show the output of the crab pyloric network in six modulatory conditions. In this species the network is silent in control saline (leftmost panel). Each modulator induces the network to produce a distinctly different output. CCAP, crustacean cardioactive peptide. Modified from Marder and Calabrese (1996). (c) Modulation can switch neurons between neural networks. Top left: A simplified pyloric synaptic connectivity diagram that also shows input from another network, the cardiac sac network (oval), and a sensory input that activates the cardiac sac network and abolishes postinhibitory rebound (PIR) in the VD neuron (leftmost connections; synaptic symbol conventions as in Figures 1 and 2). Top right: When the sensory input is silent, the VD neuron fires with the pyloric network. Bottom: After sensory input activity, the cardiac sac network becomes active (dpon trace), and the VD neuron fires with it. Modified from Hooper and Moulins (1990). Abbreviation not defined in text: IV, Inferior Ventricular.

The second role of modulation is to induce individual CPGs to assume new functional configurations that produce different motor outputs ([Harris-Warrick and Marder, 1991](#)). [Figure 3b](#) shows the output of the crab pyloric network under six modulatory conditions. In this experiment input from more central ganglia was blocked; in the crab, this results in the network becoming silent in control saline (leftmost panel). However, application of any of a variety of modulatory substances induces network rhythmicity (other five panels), and it is apparent that each substance induces the network to produce a different output. These different patterns result from the different modulators affecting different network neurons and/or having different effects on the same neuron(s). Importantly, detailed studies of one of these modulators (proctolin) in the lobster have shown that its actions cannot be understood by considering only the neurons it affects directly ([Hooper and Marder, 1987](#)). Instead, neurons that are not directly affected both alter the response of the directly affected neurons and help to transmit the changes in the

activity of these neurons throughout the network. The network has thus evolved so that, in response to changes induced in only a few of its neurons, the entire network changes its activity in a coherent, coordinated fashion; these data suggest that the functional target of modulation in this system is the network as a whole.

The third role of modulation is to alter CPG neuron complement by switching neurons between networks ([Hooper and Moulins, 1990](#); [Weimann and Marder, 1994](#)) and fusing formerly separate networks into larger entities ([Dickinson *et al.*, 1990](#)). In combination with the second role of modulation noted above, these effects dramatically increase nervous system efficiency in that, instead of needing large numbers of dedicated networks each of which performs only a single task (and whose neurons are unused except when that task is required), a single set of neurons can be used to build many CPGs, and thus to produce a wide range of motor outputs.

[Figure 3c](#) shows an example of neuron switching in the lobster stomatogastric system. The top left panel shows a simplified pyloric network and another network, the cardiac sac network (upper oval), which makes an excitatory synapse on to the pyloric network's Ventricular Dilator (VD) neuron. Also shown is a sensory input that activates the cardiac sac network and abolishes the ability of the VD neuron to express plateau potentials. The cardiac sac network is silent when this input is silent, and the VD neuron cycles with the pyloric network (top right panel). After the input is stimulated, the VD neuron no longer rebounds after pyloric inhibition, and thus no longer fires with the pyloric pattern (bottom panel). However, the cardiac sac network is now rhythmically active (extracellular recording from the dorsal posterior oesophageal nerve (dpon), which carries the Cardiac Sac Dilator (CD) neuron 1 and 2 axons), and the VD neuron fires with it because of the network's excitation of the VD neuron.

Development of Central Pattern Generation Networks

As animals mature, there are changes in the rhythmic motor patterns they express. For instance, tadpoles swim, but frogs hop; chicks hatch, but then walk; humans crawl, then walk, then run. Furthermore, humans can easily learn novel rhythmic motor patterns (e.g. swimming strokes, dances) that, once learned, seem as 'automatic' and ingrained as do clearly CPG-driven motor patterns such as walking.

How are new motor patterns acquired, and what happens to developmentally discarded motor patterns? All available evidence in vertebrates suggests that: (1) CPG development does not require movement-induced sensory feedback, or even muscle innervation; (2) later rhythmic motor patterns arise by modification of the CPGs that generated earlier patterns; and (3) the ability to produce motor patterns that are expressed at only one developmental stage (hatching) is not lost as the animal matures, but can be re-induced by applying the proper sensory input at more mature stages ([Sillar, 1996](#)). These data suggest that fundamental CPG properties are innately established, and the acquisition of new rhythmic motor patterns occurs by the CPG becoming increasingly multifunctional, presumably as a result of increasing CPG synaptic and cellular complexity, and additional extra-CPG descending input.

In these vertebrate examples, only motor pattern expression, not CPG neuron complement, can be observed. However, support for the above scenario has been provided by [Casasnovas and Meyrand \(1995\)](#), who followed lobster stomatogastric nervous system development from early embryo to adult.

All the neurons of this system are present in the early embryo, and at this stage the system produces a single, unified, rhythmic output. As the animal matures, subsets of the system's neurons segregate into different functional networks until, in the adult, the system contains three CPGs that produce different motor outputs. However, in response to appropriate sensory input, these networks can again fuse into a single network that produces a unified output. This system thus not only shows the innate development and gradual increase in complexity observed in vertebrates, but may also show the retention of developmentally early motor patterns observed in them as well.

Conclusions and Future Directions

As a result of the work since the 1960s, we have considerable understanding of how CPGs produce their neural outputs, and some understanding of how CPGs interact, how sensory feedback contributes to their activity, and how modulation increases CPG flexibility. Work continues apace to understand more fully the roles played by these aspects of motor pattern generation. Behaviour, however, consists not of spike trains, but of movement patterns that are continually adapted to match environmental variation. The role of effector characteristics (e.g. muscle dynamics, limb inertia, joint resistance) in the transformation of neural inputs into motor outputs, and how corrective sensory input is integrated into CPG activity, are relatively little understood. Therefore, a complete understanding of how CPGs generate behaviour will not be achieved until all of these issues are resolved.

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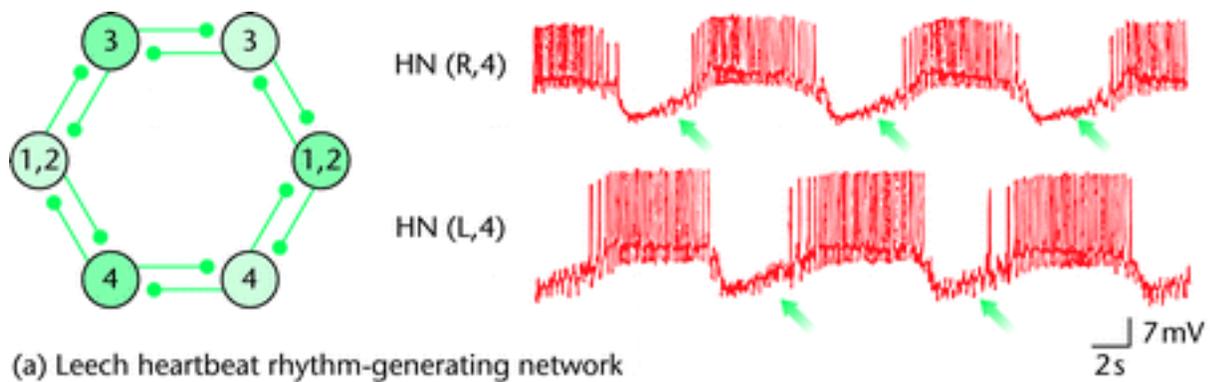
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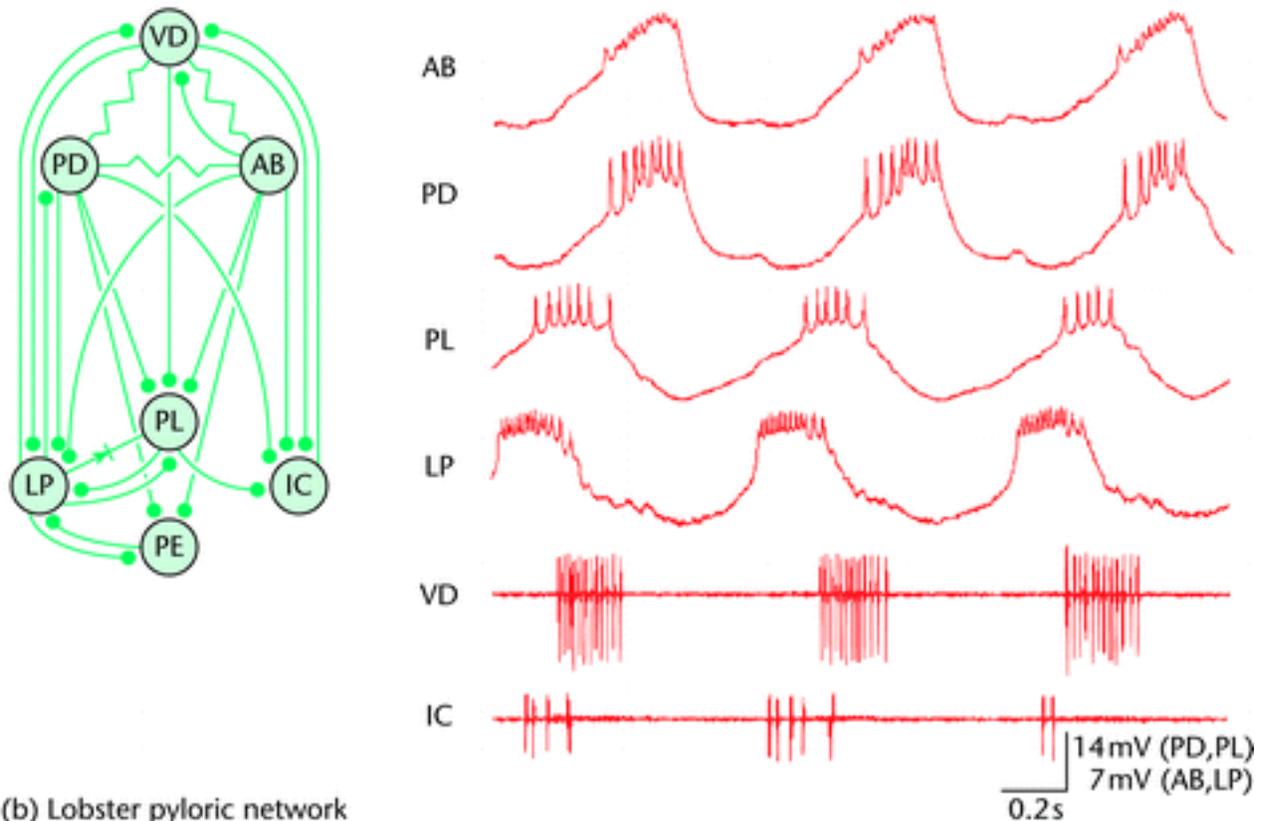
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(a) Leech heartbeat rhythm-generating network



(b) Lobster pyloric network

Figure 1 Mechanisms for central pattern generator rhythmicity. (a) Network-based rhythmicity (the leech heartbeat rhythm generator). The network (left) consists of a ring of six neurons interconnected by reciprocally inhibitory synapses (stick-and-ball connectors). Particularly important are the neuron 3 and 4 pairs, each of which forms a half-centre oscillator (see text). The neurons of each pair burst in antiphase (right). The 1 and 2 neurons form a coordinating link between the neuron 3 and neuron 4 half-centres; the network thus produces a two-phase pattern in which the open and closed neurons burst in antiphase (left). Arrows indicate the slow depolarization that allows the off-neuron to escape from inhibition (see text). Modified from Marder and Calabrese (1996). (b) A network (the lobster pyloric network) driven by an endogenous oscillator neuron. Left: The network's neuronal complement and synaptic interconnectivity (inhibitory synapses, stick-and-ball connectors; electrical coupling, resistors; rectifying electrical coupling, diode). The AB neuron is an endogenous oscillator neuron, and under most circumstances is the network's rhythmic driver. AB neuron input induces postinhibitory rebound and plateaus in its follower neurons and, as a consequence of these effects and the interactions among the follower neurons, the network produces a multiphasic rhythmic neural output (right). Left panel modified from Harris-Warrick *et al.* (1992); right panel from author's laboratory. Neurons not identified in text: VD, Ventricular Dilator; PL, Pyloric Late; PE,

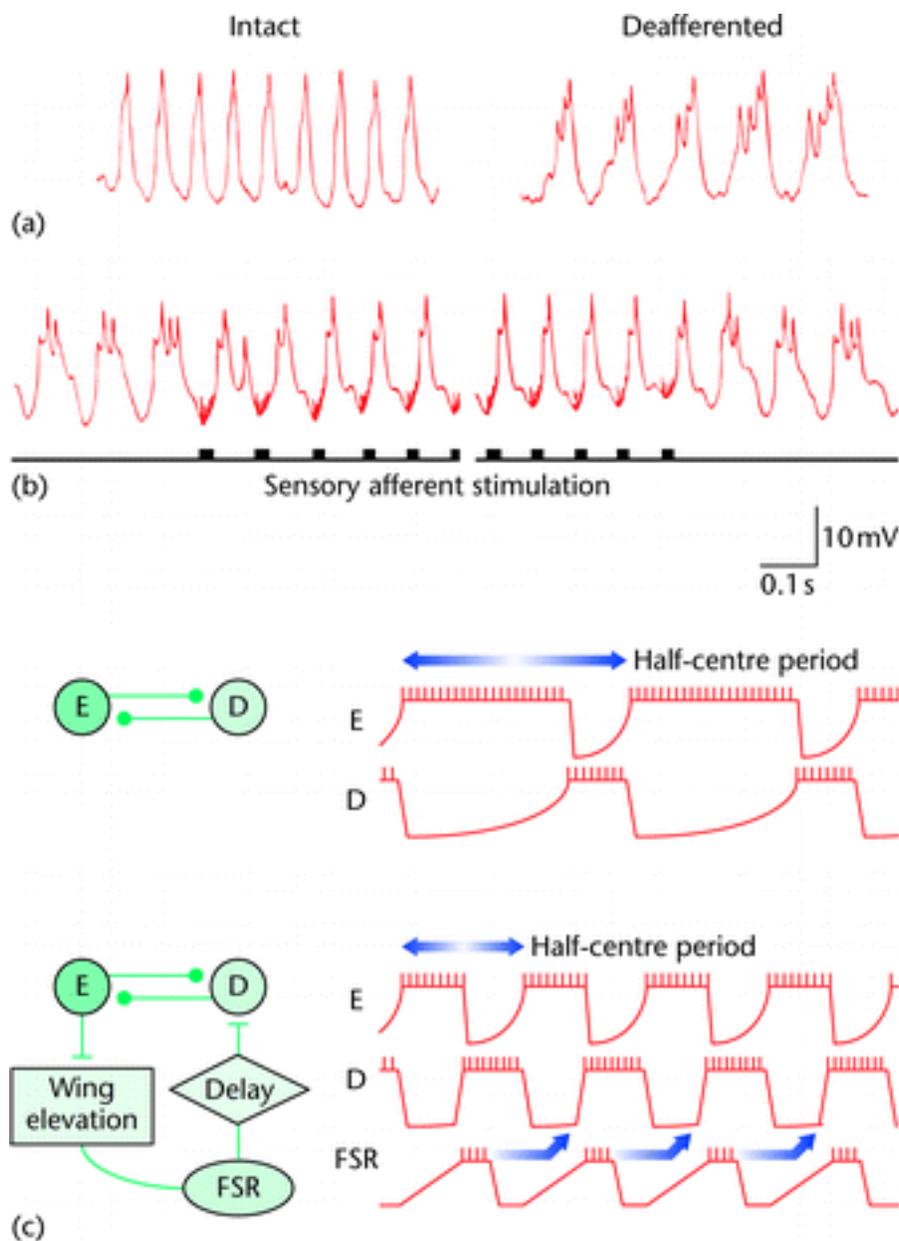


Figure 2 Sensory feedback can contribute to central pattern generator activity during normal motor pattern production. (a) Recordings of elevator motor neuron activity during locust flight with (left) and without (right) intact sensory feedback. Cycle period and burst duration increase in the deafferented preparation. (b) Sensory afferent stimulation (black rectangles on bottom trace) in deafferented locusts decreases cycle period and elevator motor neuron burst duration to near normal levels; compare with left panel in (a). (c) A simplified version of the mechanisms underlying the sensory feedback effects. The elevator and depressor interneurons form a half-centre oscillator with a long cycle period and long elevator bursts (top). Wing elevation activates a sensory receptor, the forewing stretch receptor (FSR), which excites, with a delay, the depressors (bottom). This input induces the depressors to fire earlier than they otherwise would, which decreases elevator burst duration and cycle period. Inhibitory synapses are shown with stick-and-ball connectors, excitatory synapses with stick-and-bar connectors. (a) and (b) modified from Wolf and Pearson (1988); (c) modified from Pearson and Ramirez (1990).

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Figure 3 Central pattern generator (CPG) modulation. (a) Intrinsic modulation. The *Tritonia* swimming CPG contains neurons, the DSI neurons, which, in addition to their classical synapses (green connections), release a modulator (serotonin; red arrow) (left). Sustained DSI neuron firing results in increased neuron C2 synaptic strength (middle). In response to strong sensory input (arrow) the network produces a fictive swimming pattern (right); if the serotonergic modulation is blocked pharmacologically, fictive swimming is also blocked (not shown). Inhibitory synapses, stick-and-ball connectors; excitatory synapses, stick-and-triangle connectors; mixed inhibitory–excitatory synapses are shown with a combination. Modified from Katz and Frost (1996). Neurons not identified in text: DRI, dorsal ramp interneuron; VSI, ventral swim interneuron; VFN, ventral flexion neuron; DFN-A, DFN-B, dorsal flexion neurons A and B (b) Single neural networks can produce multiple outputs. The panels show the output of the crab pyloric network in six modulatory conditions. In this species the network is silent in control saline (leftmost panel). Each modulator induces the network to produce a distinctly different output. CCAP, crustacean cardioactive peptide. Modified from Marder and Calabrese (1996). (c) Modulation can switch neurons between neural networks. Top left: A simplified pyloric synaptic connectivity diagram that also shows input from another network, the cardiac sac network (oval), and a sensory input that activates the cardiac sac network and abolishes postinhibitory rebound (PIR) in the VD neuron (leftmost connections; synaptic symbol conventions as in Figures 1 and 2). Top right: When the sensory input is silent, the VD neuron fires with the pyloric network. Bottom: After sensory input activity, the cardiac sac network becomes active (dpon trace), and the VD neuron fires with it. Modified from Hooper and Moulins (1990). Abbreviation not defined in text: IV, Inferior Ventricular.

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